I. THE INVENTION

The present invention provides, *inter alia*, systems and methods for averting undesirable pharmacokinetic drug interaction between a drug and concomitant drug(s) by controlling the *in vivo* release time and/or release site of the drug and/or the concomitant drug.

The present invention is based upon the surprising discovery that with respect to drug interaction, which is produced as a result of the drugs themselves competing for one route (for example, enzyme, carrier, *etc.*) when multiple drugs that use the same route in terms of drug absorption, distribution, metabolism or excretion are administered concomitantly, drug interaction at the route that is the problem can be averted by controlling the drug release time and/or release site with a drug delivery system. Advantageously, the systems and methods of the present invention are not only effective with regard to drug interaction between multiple drugs, but also interaction between drugs and foods.

II. REJECTION UNDER 35 U.S.C. § 103(a)

Claims 1-15 were rejected under 35 U.S.C. § 103(a) as allegedly being obvious over U.S. Patent No. 4,891,223 ("Ambegaonkar *et al.*"). According to the Examiner, Ambegaonkar *et al.* teach "a bioactive core, which can be 100% active substance or could be in admixture with an inert binder or substrate. The core has two coatings, which can control the release of the active core." Continuing, the Examiner states that it would be allegedly obvious to employ the use of any of the claimed drugs in the composition described by Ambegaonkar *et al.* in order to obtain the present invention. In response, Applicants respectfully traverse the rejection.

As set forth in M.P.E.P. § 2143:

> "To establish a *prima facie* case of obviousness, three basic criteria must be met. *First*, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. *Second*, there must be a reasonable expectation of success. *Finally*, the cited art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the cited art, not in applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991)."

Applicants assert that all three elements must be satisfied in order to establish a *prima facie* case of obviousness. Applicants assert that a *prima facie* case of obviousness has not been established for the following reasons: 1) there is no suggestion or motivation to modify the reference; 2) there is no reasonable expectation of success; and 3) the cited art reference does not teach or suggest all the claim limitations.

A. The is no Teaching or Suggestion to Modifdy the Refernece.

Applicants state that there is simply no motivation or suggestion provided in the cited reference to modify its teaching in the way the Examiner has contemplated. Obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988); *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992).

Ambegaonkar *et al.* relate to a coating formulation for a bioactive substance that results in a first-order, fractional-order, zero-order, or biphasic release of the bioactive substance (*see*, column 1, lines 6-11, Ambegaonkar *et al.*). More particularly, Ambegaonkar *et al.* relate to a bioactive composition having a controlled, sustained release delivery pattern when contacted with a suitable surrounding media comprising (a) a bioactive material core, (b) a first coating enveloping the bioactive material core, and (c) a second coating enveloping the first coating, whereby when the composition is exposed to the surrounding media, the exposure will result in the controlled release of the bioactive material (*see*, column 19, lines 37, and column 20, line 12, Ambegaonkar *et al.*).

Contrary to the teaching of Ambegaonkar *et al.*, the present invention pertains to a novel means for averting undesirable pharmacokinetic (drug) interaction between a drug and concomitant drug(s) (*e.g.*, between a drug and a food) *in vivo* in humans (*see*, page 1, lines 8-11 of the specification). As the means of averting such undesirable drug interactions, the present invention provides a drug delivery system that controls the *in vivo* release time and/or the release

site of the drug. Ambegaonkar *et al.* do ***not*** teach or suggest anything about averting undesirable pharmacokinetic (drug) interaction.

In view of Ambegaonkar *et al.*, there is simply no motivation for one of ordinary skill in the art to avert drug interaction by controlling the drug release time and/or release site with drug delivery systems and methods as is presently taught and claimed.

In view of the foregoing, Applicants respectfully request that the rejection under 35 U.S.C. § 103(a) be withdrawn.

B. There is no Reasonable Expectation of Success.

In addition, there is no reasonable expectation of success that the modification that the Examiner contemplates will succeed. "Both the suggestion and the expectation of success must be found in the cited art, not the Applicants' disclosure." *In re Dow Chem. Co.*, 5 U.S.P.Q.2d 1529, 1532 (Fed. Cir. 1988).

Ambegaonkar *et al.* do ***not*** teach or suggest anything about averting undesirable pharmacokinetic (drug) interaction.

In contrast, the present invention sets forth systems and methods for averting drug interaction in various ways. For example, the present invention relates to (a) systems and methods for averting interaction in terms of drug metabolism; (b) systems and methods for averting interaction in terms of drug absorption; (c) system and methods for averting interaction in terms of drug distribution; and (d) systems and methods for averting interaction in terms of drug excretion. These features are simply not taught or suggested in the cited art.

Applicants assert that there is absolutely no teaching or suggestion in the cited art to modify the teaching therein to arrive at the presently claimed invention. Rather, the Examiner has used the Applicants' disclosure as a blueprint to pick and choose features from the prior art in an attempt to reconstruct the presently claimed invention.

Ambegaonkar *et al.* teach a bioactive composition having a controlled, sustained release delivery pattern. The composition comprises a pharmaceutically, insecticidally, herbicidally or fertilizing core, soluble in a given surrounding media, the core present in an amount for a total dosage during a treatment period. The composition includes a first coating enveloping the bioactive material core having a polymer or a blend of polymers, wherein the

polymers swell upon penetration by the surrounding media. A second coating enveloping the first coating consisting of a polymer or a blend of polymers. The polymer or blend of polymers is water-insoluble and forms a semi-permeable barrier permitting diffusion of the surrounding media into the first coating enveloped bioactive material core and also permitting the diffusion of the surrounding media dissolved bioactive material into the surrounding media.

Ambegaonkar *et al.* do not teach or suggest averting an undesirable pharmacokinetic (drug) interaction between a drug and concomitant drug as is presently taught and claimed. In view of the foregoing, Applicants respectfully request that the rejection under 35 U.S.C. § 103(a) be withdrawn.

C. The Cited Art Does Not Teach All the Claim Limitations

The cited art references must teach or suggest all the limitations of the claims. *In re Wilson*, 165 U.S.P.Q. 494, 496 (C.C.P.A. 1970). Applicants assert that the cited art reference does not teach or suggest all the limitations of the claims and therefore, the obviousness rejection in untenable.

The drug delivery systems disclosed by Ambegaonkar *et al.* provide controlled, sustained release, particularly zero-order release, which causes the drug to be released at a uniform rate. The systems of Ambegaonkar *et al.* are limited, however, because they cannot avert the undesirable pharmacokinetic (drug) interaction between a drug and concomitant drugs(s).

Thus, the present invention, which relates to systems and methods for averting undesirable pharmacokinetic drug interaction between a drug and concomitant drug(s), by controlling the *in vivo* release time and/or release site of the drug and/or the concomitant drug, is not obvious in view of Ambegaonkar *et al.* Again, Ambegaonkar *et al.* do not teah or sughgest averting the undesirable pharmacokinetic (drug) interaction between a drug and concomitant drug as is presently taught and claimed. Under *In re Wilson supra*, a *prima facie* case of obviousness has not been established because each of the limitation of the claims is not taught or suggested in the cited art reference.

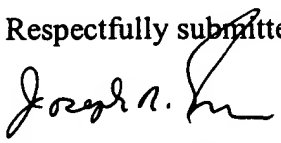
Therefore, Applicants respectfully request that the rejection under 35 U.S.C. § 103(a) be withdrawn.

III. CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 925-472-5000.

Respectfully submitted,



Joseph R. Snyder
Reg. No. 39,381

TOWNSEND and TOWNSEND and CREW LLP
Two Embarcadero Center, 8th Floor
San Francisco, California 94111-3834
Tel: (415) 576-0200
Fax: (415) 576-0300
JS:slw
WC 9042458 v1